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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,455	RAOULT, DIDIER M	
	Examiner	Art Unit	
	JaNa Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15,17 and 19-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15, 17 and 19-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. The amendment filed March 22, 2010 has been entered. Claims 15, 22 and 25. Claims 1-14, 16 and 18 have been cancelled. Claims 15, 17 and 19-25 are under consideration in this office action.

Withdrawal of Rejections

3. The following rejections have been withdrawn in view of applicants' amendments:

a) The rejection of claims 20, 22 and 24 under 35 U.S.C. 112, second paragraph;

b) The rejection of claims 15-21 and 24-25 under 35 U.S.C. 103(a) as being unpatentable over Dorval et al., in view of Hanke; and

c) The rejection of claims 22-23 under 35 U.S.C. 103(a) as being unpatentable over Dorval et al., (US Patent 5,561,045) and Hanke (DE 100 00322) in view of La Scola et al.

Response to Arguments

4. Applicant's arguments with respect to claims 15, 17 and 19-25 have been considered but are moot in view of the new ground(s) of rejection.

New Grounds of Rejection Necessitated By Amendments

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 15, 17, 19-21 and 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dorval et al., (US Patent 5,561,045) and Mattiasson (American Chemical Society Symposium Series. 1979. Vol. 106, Chapter 14, pp 2-3-220) in view of Hanke (DE 100 00 322A1, see the machine translation document from the EPO, pages 1-11).

Claim 15 is drawn to an in vitro serological diagnosis method for detecting the presence of antibodies specific to an infectious microbial agent in a sample to be tested, which comprises: a) depositing on a solid substrate a first antigen Ag_1 comprising a whole *Staphylococcus aureus* bacterium which comprises protein A and at least one second antigen Ag_2, wherein said second antigen Ag_2 is an infectious microbial agent, and b) contacting said first antigen Ag_1 and said at least one second antigen Ag_2 with a sample to be tested causing said first antigen Ag_1 and said at least one second Ag_2 to react with a sample to be tested, and c) detecting whether a human immunoglobulin Ac_1 in said human serum reacts with said first antigen Ag_1 by causing the reaction product Ag_1- Ac_1 to react with a detection substance, wherein said detection substance reacts with said human immunoglobulin and not with said first antigen (Ag_1), and wherein the reaction product Ag_1-Ac_1 is formed from the reaction of said human immunoglobulin Ac_1 and said first antigen Ag_1, and d) providing a controlled sample containing a human serum to be tested for detecting whether said human immunoglobulin react with said first antigen.

Claim 17 is drawn to the anti-human immunoglobulin being goat immunoglobulin or chick immunoglobulin. Claim 19 is drawn to the method further comprising: performing a series of tests at increasing dilutions of the sample to be tested with the detection substance Ac_1, wherein the detection substance Ac_2 is an immunoglobulin conjugated with a fluorescent substance, and verifying whether a reaction product Ag_1-Ac_1-Ac_2 can be detected by fluorescence at a dilution of the sample to be tested of 1/200 or less, wherein the reaction product Ag_1-Ac_1-Ac_2 is formed by the reaction of the human immunoglobulin Ac_1, the first antigen Ag_1, and the detection substance Ac_2. Claim 20 is drawn to the infectious microbial agent of Ag_2 being selected from a bacterium, a virus, a parasite or a fungus. Claim 21 is drawn to the second antigen being an intracellular bacterium or a virus. Claim 24 is drawn to Ag_2 is H.I.V.

Claim 25 is drawn to a diagnosis kit for detecting the presence of antibodies specific to an infectious microbial agent in a sample to be tested, which comprises: a solid substrate comprising a second antigen Ag_2 which is an infectious microbial agent, one positive controlling inclusion comprising a human serum in the sample to be tested which comprises a first antigen Ag_1 containing a whole *Staphylococcus aureus* bacterium containing protein A, and at least one reagent which can detect the presence of a reaction product of said first antigen with a human immunoglobulin Ac_1 comprising a detection substance Ac_2 which comprises a labeled immunoglobulin which is an anti-human immunoglobulin which does not react with protein A.

Dorval et al., teach processes that permit the ability to detect simultaneously a variety of classes of immunoglobulin specific for the same analyte (col.2, lines 30-34).

Dorval et al., teach the enhancement of sensitivity using specific binding proteins like Protein A within immunoassays (col. 2, lines 35-40). Dorval et al., teach anti-IgA-IgG and anti-IgM-IgG and protein A (col. 3, lines 19-20). Dorval et al., teach a solid support with a first antigen containing Protein A, a second microbial antigen, the addition of the detection agent which is labeled anti-human immunoglobulin with does not react with Protein A, see Figures 1a-1f. Dorval et al., teach a variety of kits with include the detection reagents, the binding protein A, and immunoglobulins (col. 4, lines 40-49). Dorval et al., teach labels to be chromophores, fluorophores, metal sols, enzyme labels and colorimetric particles (col. 6, lines 48-68). It is noted, that fluorescein is a common type of fluorophore. Dorval et al., teach the sensitivity of a wide variety of assays is enhanced with the use of the immunoglobulin and Protein A, including direct, indirect, competitive and sandwich type heterogeneous and homogenous assays (col. 9, lines 16-25). Dorval et al., teach the reagents may be advantageously in virtually any type of immunoassay where it is desirable to prevent the interaction of Protein A with a portion of an immunoglobulin; thus allowing the antigen to be bound to a solid phase and the presence of different classes of specific antibodies to be determined (col. 9, lines 25-33). Dorval et al., teach the detection of HIV virus (col. 9, lines 37-42). However, Dorval et al., do not specifically teach immobilization of a whole S. aureus bacterium or teach the second antigen being *Bartonella* or a bacterium being responsible for endocarditis.

Mattiasson teaches application of immobilization of whole cells in analysis (page 203). Mattiason teach advances in immobilization techniques for whole cells and the increasing range of applications of modern enzyme based analyses will lead to a wider

use of immobilized organelle and whole cells (page 203). Mattiasson teaches the cell surface being the subject of increasing attention where many specific properties of various cells can be explained by the presence of specific molecules on the cell surface (page 213). Staphylococcus aureus is an example of bacteria carrying specific molecules called protein A, which has specific binding properties since it binds immunoglobulin subgroups I, II and IV via their Fc fragments. Also it is well known it be used in enzyme immunoassays (page 215). Mattiasson teaches the immobilization of cells for studying viruses as well (page 215)The techniques for handling immobilized cells is easy, well controlled and sensitive in biospecific analytical systems (page 217).

Hanke teaches strips for western blotting which include on a carrier, (i) a serum control zone which will produce a band flowing incubation with patient serum and (ii) at least one conjugate control zone which will produce a band following incubation with a labeled anti-patient immunoglobulin antibody from a different animal species (abstract). Hanke teaches multiple control zones which make for improved differentiated, additional control possible and provides improved interpretation of test results (page 1 of the translation). Hanke teaches a labeled conjugated animal antibody which is specific for human immunoglobulin (page 2).

Therefore, it would have been prima facie obvious at the time of applicants invention to modify the *in vitro* serological diagnosis method in which, in a sample to be tested, the presence is detected of antibodies specific to an infectious microbial agent, as taught by Dorval et al., wherein the modifications incorporate using deposited whole S. aureus bacterium comprising protein A as taught by Mattiasson and the use a control

zone as taught by Hanke in order to provide a method that establishes detection of human immunoglobulin interaction. Furthermore, there is a reasonable expectation of success in incorporating the methods of Dorval et al., Mattiasson and Hanke since they teach providing a sample to be tested is react with solid-substrate having a deposited first and second antigen and detecting whether the human immunoglobulin reacts with the antigen, especially when no change in their respective functions, thus the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Furthermore, one of ordinary skill in the art at the time the invention was made would have been motivated to extend the methods taught by Dorval et al., Mattiasson and Hanke while incorporating the additional whole cell bacterial and viral pathogens into the *in vitro* serological diagnosis as in order to arrive at the claimed invention with provide assays containing serum and conjugate control zones when detecting infectious microbial antigens.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 15, 20 and 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dorval et al., Mattiasson and Hanke as applied to claims 15 and 20

above, and further in view of La Scola et al (Journal of Clinical Microbiology, 1996; 34(9): 2270-2274).

Claim 22 is drawn to the second antigen being Chosen from among bacteria of the genus *Rickettsia, Coxiella, Bartonella, Tropheryma, Ehrlichia, Chlamydia, Mycoplasma, Treponema, Borrelia,* and *Leptospira.* Claim 23 is drawn to the second antigen corresponding to the infectious microbial agent is a bacterium responsible for endocarditis.

Dorval et al., Mattiasson and Hanke have been discussed above, however neither teach the second antigen being *Bartonella* or a bacterium being responsible for endocarditis.

La Scola et al, teach serological cross-Reactions *between Bartonella Quintana, Bartonella henselae,* and *Coxiella burnetti. Bartonella Quintana,* is known to be associated with endocarditis, while *Bartonella henselae* is known to be associated diseases in AIDS patients (page 2270).La Scola et al., teach a method of performing serological diagnostic test for *Bartonella* and *C. burnetti* infections (page 2270). The prior art discloses immunoglobulin G (IgG) anti-phase I titer of equal to or greater than 1:800 and an IgA anti-phase II titer were considered diagnostic for infection. La Scola et al teach that human patients with titers of equal to or greater that 1:1,600 or antibody against *B. henselae* or *B. Quintana* antigens were also considered diagnostic for infection (page 2272). La Scola et al., teach positives being found (IgG, 1:100) (IgG 1:200) (page 2271). The method of La Scola et al comprises the following steps: a) Serum samples were taken from patients; b) Bacterial antigen being deposited on 30

well microscope slides, and sera was serially diluted and applied to the wells; c) Slides were incubated in a moist chamber for 30 minutes, washed, dried and overlaid with labeled goat anti-human IgG antibodies; d) Interaction of antigen and antibody was observed (page 2271). La Scola et al., teach Western blotting was used to determine the interaction of antigen and antibody (page 2271).

Therefore, it would have been prima facie obvious at the time of applicants invention to modify the *in vitro* serological diagnosis method in which, in a sample to be tested, the presence is detected of antibodies specific to an infectious microbial agent, as taught by Dorval et al., and Hanke wherein the modification incorporates the use of variety of microbial agents as taught by La Scola et al., in order to provide detection of a wide variety of agents. Furthermore, there is a reasonable expectation of success in incorporating the methods of Dorval et al., and Hanke in view of La Scola et al., since both teach providing a sample to be tested is react with solid-substrate having a deposited first and second antigen and detecting whether the human immunoglobulin reacts with the first antigen, especially when the steps and components of the method have been combined with no change in their respective functions, thus the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to extend the methods taught by Dorval et al., and Hanke while incorporating the additional yet equivalent microbial antigens associated with AIDS and HIV into the *in vitro* serological diagnosis as taught by Dorval and Hanke in

order to arrive at the claimed invention with provide enhanced sensitivity using specific binding proteins like Protein A within immunoassays.

Conclusion

7. No claims allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached Monday thru Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Robert Mondesi, can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/JaNa Hines/
Examiner, Art Unit 1645

/Mark Navarro/
Primary Examiner, Art Unit 1645